EDEXCEL Advanced Level

Edexcel IAL Biology Unit 1

Summary©

HASAN SAYGINEL

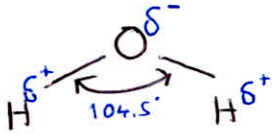
HS

Topic 1: Lifestyle, health and risk

Chemistry of water

Water is essential for life. The importance of water is due to the basic chemistry of its molecules.

Water molecule:



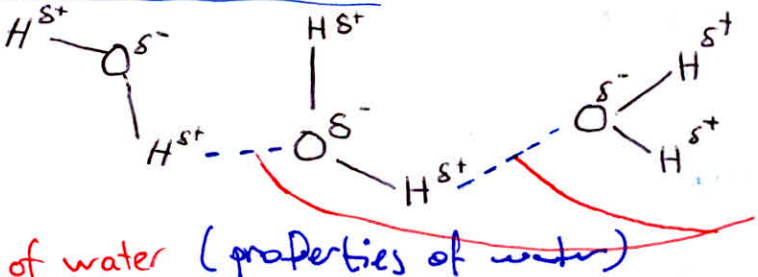
δ⁻ : weak negative charge

δ⁺ : weak positive charge

Each water molecule is slightly polarized. Water molecules are dipolar, because it has a very slightly negative part (the oxygen atom) and very slightly positive parts (hydrogen atoms). One of the most important results of this charge separation is that water molecules form hydrogen bonds.

Hydrogen bond: A relatively weak link between two atoms in which a weakly negative atom attracts another weakly positive atom.

Hydrogen bonds in H_2O molecules:



Importance of water (properties of water)

1. Water is an unusual and excellent solvent.
2. Water has one of the highest known surface tensions.
3. The water molecule is amphoteric.
4. good transport medium
5. High specific heat capacity

Water as a solvent

Many substances are soluble in water. The fact that the water molecule has a dipole means that many ionic substances, which are made up of positive and negative ions, will dissolve in it. Water dissolves many substances that organic solvents do not. Water also dissolves many non-polar substances. These substances may form colloids.

- Colloid: A mixture in which very small particles of one substance are distributed evenly throughout another substance. The solute particles of a colloid are larger than the particles of the solvent.

Particles that are insoluble in water form emulsions or suspensions.

- Emulsion: Tiny droplets of one liquid suspended in another liquid.
- Suspension: A solid mixed with a liquid in which the particles will separate out if the mixture is not constantly moved or stirred.

* Water is important as a solvent in transport. For example;
  - → Plasma is a solution
  - → Cytoplasm is a colloid
  - → Blood is a suspension.

* The properties of solutions, colloids and suspensions adapt these biological materials to carry out their functions in the body.

Organic Compounds in living things

Organic compounds are the ones that contain carbon atoms. Most living things are made of organic molecules, apart from water. Carbon atoms can make four bonds and can bond with each other too, so they can make long chains, with other atoms such as hydrogen and oxygen. The carbon atoms may also bond to form branched chains, rings or even three-dimensional shapes.

Carbohydrates

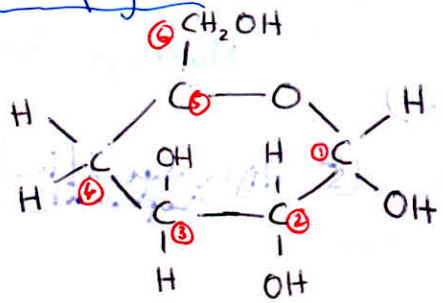
Carbohydrates are important in organisms as an energy source. There are three main groups of carbohydrates: monosaccharides, disaccharides and polysaccharides.

Monosaccharides

The monosaccharides are known as the simple sugars. They have the general formula $(CH_2O)_n$. They include:

- trioses ($C_3H_6O_3$)
- pentoses ($C_5H_{10}O_5$) e.g ribose and deoxyribose
- hexoses ($C_6H_{12}O_6$) e.g glucose, fructose, galactose

Structure of α-glucose



α-glucose is a hexose and hexose sugars have a ring structure.

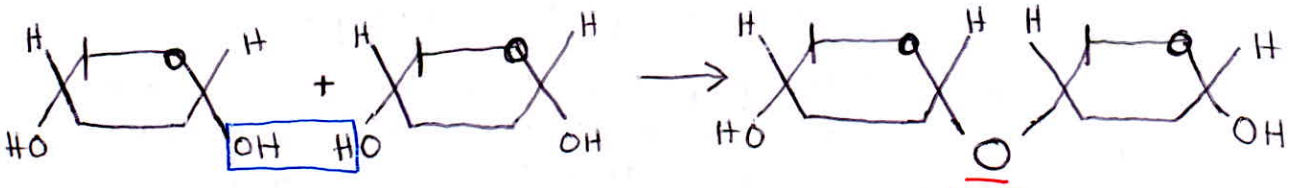
Disaccharides

Disaccharides are made up of two monosaccharides joined together. Two monosaccharides are linked together by a glycosidic bond during a condensation reaction.

- Glycosidic bond: A covalent bond between two monosaccharides.
- Condensation reaction: A reaction in which two molecules are linked together with the elimination of a molecule of water.

* When different monosaccharides join together, different disaccharides result:
  - sucrose = glucose + fructose (Stored in plants such as sugar cane)
  - lactose = glucose + galactose (The main carbohydrate in milk)
  - maltose = glucose + glucose (Found in germinating seed such as barley)

The formation of a glycosidic bond



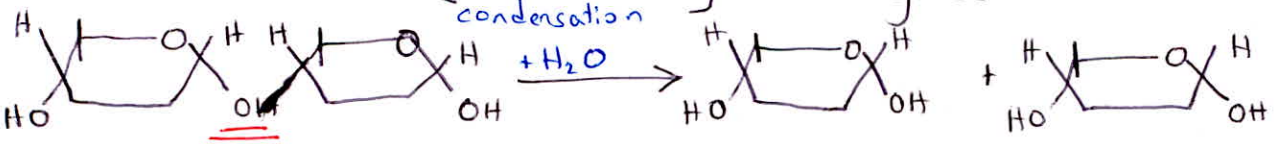
1,4 glycosidic bond

Hydrolysis reactions

A hydrolysis reaction is a reaction in which a molecule of water is used in breaking a chemical bond. (the reverse of a condensation reaction). To be useful as an energy store the bonds in carbohydrates need to be broken to release single sugars for cells to use. Disaccharides can be split to form two monosaccharides, and the same reaction is used to gradually break down starch and glycogen into shorter and shorter chains.

Hydrolysis of maltose

maltose + water ⇌ (hydrolysis / condensation) glucose + glucose



1,4 glycosidic bond is broken

Polysaccharides

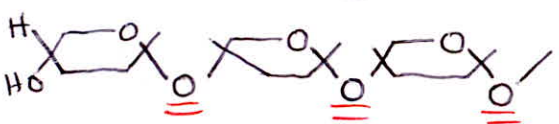
A polysaccharide is built from many monosaccharides linked by glycosidic bonds formed during condensation reactions. There are three main polysaccharides – starch, glycogen and cellulose. Starch and glycogen are involved in providing and storing energy whereas cellulose has a structural role.

* Starch

Starch is a mixture of two polysaccharides, both of which are polymers of α - glucose:

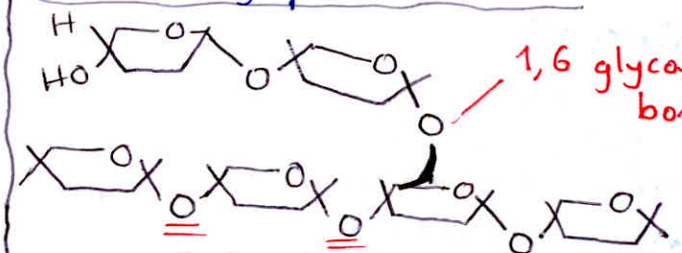
- **Amylose:** is an unbranched polymer. As the chain lengthens the molecule spirals, which makes it more compact. The glucose molecules can only be released by enzymes working from each end of the amylose molecule.
- **Amylopectin:** is also a polymer of glucose molecules but the amylopectin chains branch. These branching chains have lots of terminal (end) glucose molecules that can be broken off rapidly when energy is needed

Amylose



1,4 glycosidic bonds

Amylopectin



1,6 glycosidic bond

1,4 glycosidic bonds

* Starch is the major storage carbohydrate of most plants. It is laid down as compact grains. It is useful because its molecules are both compact and insoluble, but are readily hydrolysed to form sugar when required. Of course, enzymes are involved in the reaction, too.

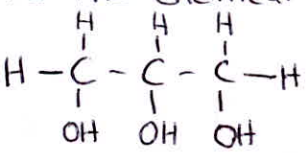
* Glycogen

Glycogen is the only carbohydrate energy store found in animals. Chemically it is very similar to starch (amylopectin), being made up of many α-glucose units. Like starch it is a compact molecule. However, the glycogen molecule has many side branches that are linked with a 1-6 glycosidic bond. This means it can be broken down very rapidly. This makes it an ideal energy store for very active tissues such as muscle and liver tissue, which need a readily available energy supply at all times.

Lipids

Fats and oils are important groups of lipids. Chemically they are extremely similar, but fats are solid and oils are liquid at room temperature. Like carbohydrates, they are organic molecules. They are made up two types of organic chemicals, fatty acids and glycerol.

- Glycerol has the chemical formula $C_3H_8O_3$.



- All fatty acids have a long hydrocarbon chain - a pleated backbone of carbon atoms with hydrogen atoms attached, and a carboxyl group (-COOH) at one end. The length of the carbon chain differs. The fatty acid may be saturated or unsaturated.

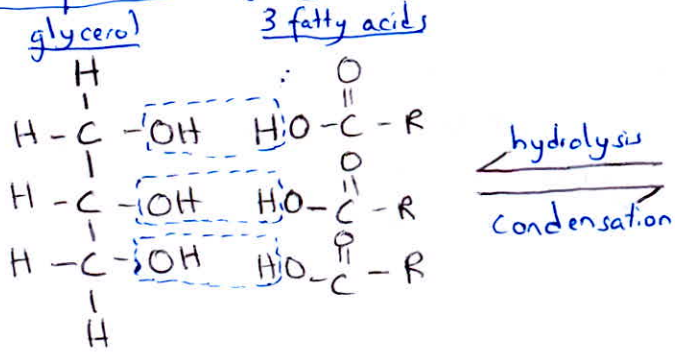
→ Saturated fatty acid: One in which all the bonds between carbon atoms in the hydrocarbon chain are single covalent bonds. (C-C)

→ Unsaturated fatty acid: ~~One in which all the bonds between~~ A fatty acid in which one or more pairs of adjacent carbon atoms in the hydrocarbon chain are linked by a double covalent bond. A monounsaturated fatty acid has one double bond and a polyunsaturated fatty acid has more than one double bond. A monounsaturated fatty acid has a straight chain ~~whereas a poly~~ with only one kink at the double bond and a polyunsaturated fatty acid has more than one.

Triglycerides

Triglycerides are formed during condensation reactions between glycerol and three fatty acids. The bonds formed are known as ester bonds. Triglycerides are the most common kind of lipids.

* Esterification - Hydrolysis



28.09.15

Proteins

Proteins make up about two-thirds of the total dry mass of a cell. These organic molecules differ from carbohydrates and lipids in that they contain the element nitrogen, and often the element sulfur, as well as carbon, hydrogen and oxygen. Proteins are polypeptide chains made up of amino acids that are joined together by peptide bonds.

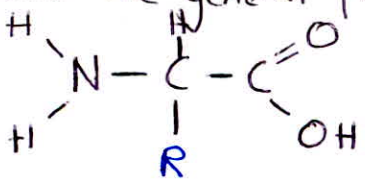
-Amino acid: The monomer from which dipeptides, polypeptides and proteins are made.

Amino acids

All amino acids contain two functional groups:

- an amino group ($-NH_2$)
- a carboxyl group ($-COOH$)

and have the general formula:



R represents the only part of the molecule that is different in different amino acids.

Note: Molecules, like amino acids, that can ionise as both and acid and a base are described as being amphoteric and an ion with both positive and negative charges is called a zwitterion. The amino group is basic and the carboxyl group is acidic.

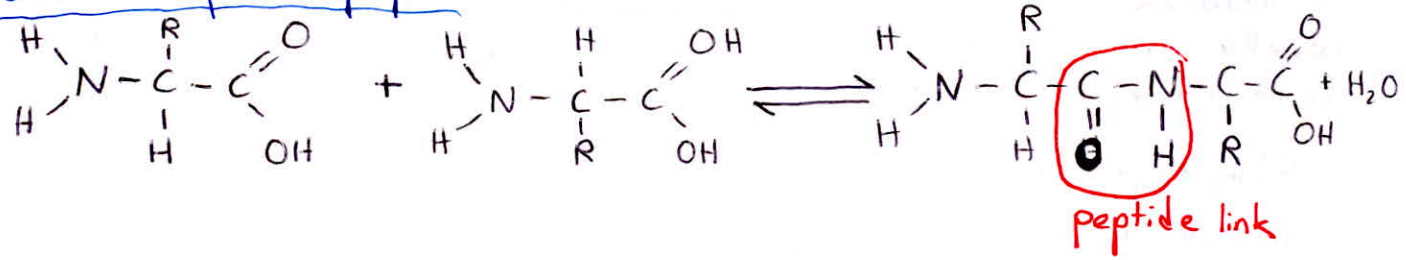
Formation of polypeptides and proteins

In the presence of an enzyme, two amino acids combine in a condensation reaction with the elimination of water. During this reaction, a peptide bond forms.

-Peptide bond: A covalent bond between the amino group of one amino acid and the carboxyl group of other amino acid. Each peptide bond is formed by a condensation reaction.

→ Further condensation reactions result in polypeptides with the addition of one amino acid each time.

Formation of a dipeptide



The structure of proteins

There are four levels of protein structure: primary, secondary, tertiary, quaternary (type number &)

(1) The primary structure of a protein is the sequence of amino acids in its molecule. The amino acids are held together by peptide bonds. Proteins differ in variety, number and order of their constituent amino acids. Note: Just changing one amino acid in the sequence might completely alter the properties of a protein.

(2) The secondary structure of a protein develops immediately after its formation when parts of the polypeptide chain become folded or twisted, or both. (consider the type of bonds responsible for it. Structure.)

(3) The tertiary structure of a protein is the compact structure, unique to that protein, that arises when the molecules is further folded and held in a particular complex three-dimensional shape.

(4) The quaternary structure of a protein arises when two or more polypeptides become held together, forming a complex, biologically active molecule

Other bonds in proteins

Along with peptide bonds, there are some other bonds which are much weaker in the 3D structure of a protein. They keep the 3D structure in place. They include hydrogen bonds, sulfur bridges and ionic bonds.

- Hydrogen bonds: They are formed by the attraction of slightly negative charges on the oxygen of the carboxyl groups and slightly positive charges on the hydrogen atoms of the amino groups. They are very important in the foiling and coiling of polypeptide chains.
- Sulfur bridges: Strong covalent bond formed by the oxidation of -SH groups of two cysteine side chains.
- Ionic bond: Electrostatic interaction between positively and negatively charged ions

Fibrous and globular proteins

Fibrous proteins

Fibrous proteins have little or no tertiary structure. They are long, parallel polypeptide chains with hydrogen bonds that form into fibres. This structure is resistant to denaturing and strengthened, which makes such proteins ideally suited to their usual structural functions within organisms. Collagen is an example of a fibrous protein.

Globular proteins

Globular proteins have complex tertiary and quaternary structures. They are more spherical. Their polypeptide chains wind in such a way that their hydrophilic amino acids are at the surface of the sphere whilst their hydrophobic amino acids are at its core. They form colloids. Enzymes and hormones are examples of globular proteins.

Enzymes

Enzymes are organic catalysts that speed up a metabolic reaction in cells and organisms. A metabolic reaction may be classified as one of just two types:

- In anabolic reactions, larger molecules are built up from smaller molecules.
- In catabolic reactions, larger molecules are broken down

Overall: metabolism = anabolism + catabolism

Enzymes as catalysts

Enzymes are biological catalysts, with each enzyme catalysing only a specific reaction or group of reaction. They show great specificity. Enzymes are proteins and they have a very specific shape as a result of their tertiary and quaternary structures, and this means they can only catalyse specific reactions.

An enzyme molecule works by binding to a specific substance, known as its substrate molecule, at a specially formed pocket in the enzyme, called its active site.

-Active site: The active site is the small part of the enzyme molecule that binds to its specific substrate and caues the catalysis.

There are two suggested models that represent the action of enzymes:

- Lock-and-key hypothesis
- Induced-fit hypothesis

substrate + enzyme $\rightleftharpoons$ enzyme-substrate complex $\rightleftharpoons$ enzyme + products

Lock-and-key hypothesis

In this model, the enzyme and substrate molecules have a fixed shape and the substrate fits into the active site of the enzyme just like a key fits into a lock and enzyme-substrate complex forms.

Induced-fit hypothesis

This is the modification of the previous model. According to this hypothesis, when an enzyme and substrate combine, the enzyme's active site changes shape to become truly complementary to the part of the substrate to which it attaches. Combination with its substrate induces the enzyme's active site to fit.

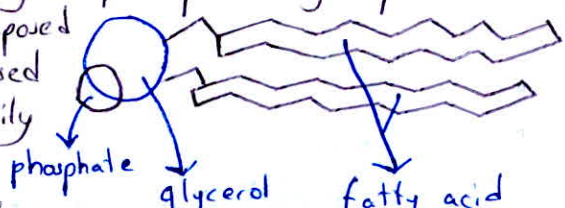
Enzymes and activation energies

Enzymes catalyse reactions by lowering the activation energy needed by a reaction to occur. Activation energy: The energy barrier that must be overcome before reactants reach their temporary transition state. Enzymes lower the activation energy of the reactions they catalyse, making the reaction occur more readily.

**Note: Most enzymes work within cells, in other words they are intracellular. Some, like the enzymes of our own digestive system or of microorganisms that cause the recycling of nutrients within the ecosystem are secreted from the cell which means they are extracellular.

Phospholipids

A phospholipid has a similar chemical structure to a triglyceride, except one of the fatty acid groups is replaced by a phosphate group.



A phospholipid molecule has a head composed of a glycerol to which is attached an ionised phosphate group. Since hydrogen bonds readily form between this phosphate group and water molecules, this part of the molecule has hydrophilic properties. The remainder of a phospholipid consists of two long, fatty acid residues, comprising hydrocarbon chains. These tails have hydrophobic properties. Therefore, phospholipids are amphipathic.

- Hydrophilic: Refers to substances that will mix with water (water-loving).
- Hydrophobic: Refers to substances that will not mix with water (water-hating).

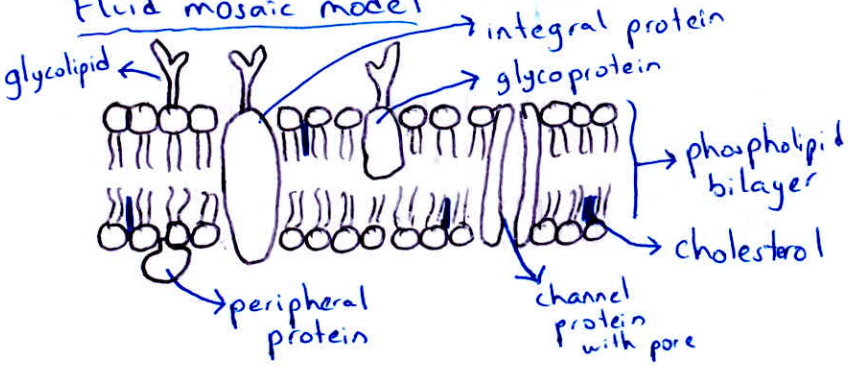
* Phospholipid molecules in contact with water form a monolayer, with heads dissolved in the water and the tails sticking outwards.
* When mixed with water, phospholipid molecules rearrange themselves into a bilayer, in which the hydrophobic tails are attracted to each other.

- Bilayer: A single structure made of two layers of molecules, usually used to describe the arrangement of phospholipids in a cell membrane.

The Structure of the cell surface membrane

Fluid mosaic model is the currently accepted model of the structure of the cell membrane which suggests ~~the surface of~~ it is mainly comprised of a phospholipid bilayer, with many proteins and other molecules floating within it, whilst others are fixed in place

Fluid mosaic model



- Glycoprotein: Protein with a carbohydrate prosthetic group. Their functions have since been shown to be cell-cell recognition, or as receptor sites for chemical signals. others are involved in the binding of cells into tissues.

- Integral proteins: Proteins present in the cell surface membrane that are partially or totally buried within the lipid bilayer.
- Peripheral proteins: Proteins present in the cell surface membrane that are superficially attached to the lipid bilayer.

* The proteins of cell surface membranes are globular proteins. One of the main functions of the membrane proteins is to help substances move across the membrane. The proteins may form pores or channels which allow specific molecules to pass.

Transport Across Membranes

Molecules, atoms and ions move through membranes in three main ways:

- Movement by passive transport (diffusion and osmosis)
- Movement by active transport
- Movement by bulk transport

Movement by passive transport

Passive transport – Transport that does not require energy. Diffusion and osmosis are forms of passive transport.

Diffusion

Diffusion is the net movement of the molecules of a fluid from a region of their high concentration to a region of low concentration. Molecules move down their concentration gradient.

* Diffusion occurs because of the random motion of molecules due to the kinetic energy they have, which is dependent on their temperature.

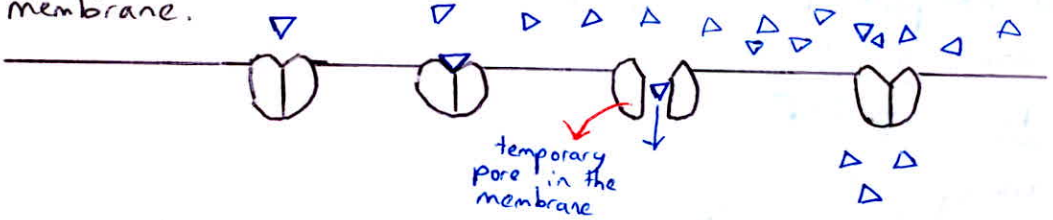
Small molecules like O_2 and CO_2 diffuse freely across cell surface membranes. However, larger hydrophilic molecules and ions cannot.

-Facilitated diffusion

Facilitated diffusion is a specialised form of diffusion in which there is a net movement of ~~a field~~ molecules from a region of their high concentration to a region of low concentration through channel proteins.

Note: In facilitated diffusion, the energy comes from the kinetic energy of the molecules involved, as is the case in all forms of diffusion.

Note: Channel proteins are specific to one particular molecule/ion. Some channels open when a specific molecule is present or there is an electrical charge across the membrane.



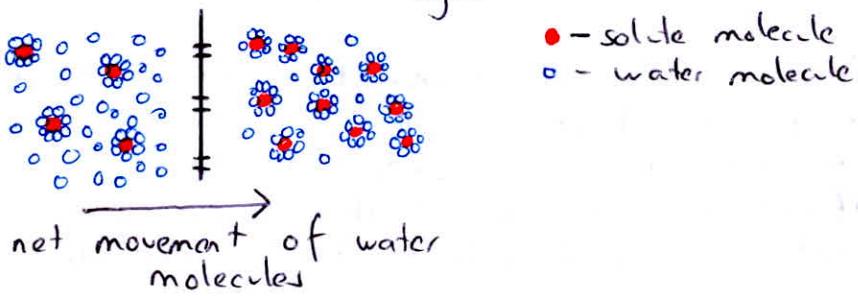
→ The channel protein changes shape when the particular ion/molecule is detected and allows the substance to diffuse across it. Then, it returns back to its original shape.

* An important example of facilitated diffusion is the movement of ADP into and out of mitochondria.

Osmosis

Osmosis is the movement of solvent molecules (water) from a region of their high concentration to a region of low concentration through a partially permeable membrane. Osmosis is a special case of diffusion and does not require energy from metabolism.

Diffusion of water is from a dilute solution to the more concentrated solution. This is because ~~solute~~ particles like amino acids, polypeptides, proteins and inorganic ions attract polar water molecules. These form weak chemical bonds with water molecules, including hydrogen bons. Therefore, movement of water molecules is restricted. In a dilute solution there are more free water molecules so they diffuse from that region to the more concentrated region.



- Osmosis and living cells

→ Osmosis needs to be carefully controlled in animal cells, as they might burst in too much water or they might shrink in too little water.

→ Plant cells, however, have cell walls which are made of cellulose and prevent bursting. Cytoplasm swells when too much water enters the cell. This increases the inward pressure of the cell wall on the cytoplasm until it cancels out the tendency for water molecules to move in. At this point the plant cell is fully turgid.

Movement by active transport

Active transport: The movement of substances across a cell surface membrane against a concentration gradient using energy in the form of ATP.

*The Role of ATP

The energy needed for active transport is provided by molecules of adenosine triphosphate (ATP). The ATP is produced during cellular respiration. The active transport carrier system in the membrane involves the enzyme ATPase. The enzyme catalyses the breakdown of ATP, removing a phosphate group to form adenosine diphosphate (ADP). Energy is released by the breaking of this bond, and this energy may be used to move the carrier system in the membrane or to release the transported substances and return the system to normal.

Mechanism of active transport

Active transport involves a carrier protein which often spans the whole membrane. It may be very specific, picking up only one type of ion or molecule, or it may work for several relatively similar substances.

Steps (glucose as an example)

- Glucose molecules (specific shape) arrive at carrier proteins.
- Carrier protein changes shape to allow glucose molecules into the cell. This requires energy in the form of ATP. $ATP \rightarrow APP + Energy$
- Glucose molecules are carried across membrane in carrier protein of matching shape.
- Protein carrier returns to original shape to allow more glucose molecules to enter.

* In active transport the movement of a substance is often linked with that of another particle, such as a sodium ion. One of the best known examples of active transport is the 'sodium pump' that actively moves potassium ions into the cell and sodium ions out.

Movement by bulk transport

Large particles cannot enter or leave a cell using membrane transport systems. However, the membrane has properties that make it possible to move larger particles into or out of the cell. This bulk transport occurs through the movement of vesicles of matter. Vesicles are membrane-bound cell organelles containing liquid or solid particles.

Endocytosis

Endocytosis is the movement of materials into cells.

Endocytosis

- uptake of solid particles = phagocytosis
- uptake of liquid particles = pinocytosis

Exocytosis

Moving substances out of a cell by emptying a membrane-bound vesicle.

Note: The strength and flexibility of the fluid mosaic membrane makes this activity possible. Energy from metabolism (ATP) is also required to bring it about.

07/10/15

Transport in Large organisms

In contrast to unicellular organisms such as an Amoeba, larger organisms are made up of billions of cells. Such unicellular organisms do not require a circulation system as diffusion is enough for them. The surface area to volume ratio of unicellular organisms is large, so substances can be easily diffuse in and out of them.

On the contrary, many animals (large, multicellular organisms) have a heart and circulation to overcome limitations of diffusion. Nutrients and respiratory gases would otherwise reach the cells not fast enough to sustain the processes of life.

In humans, this transport system is the heart and circulatory system and the blood which flows through it. This is an example of mass transpat system where substances are transported in the flow of a fluid with a mechanism for moving it around the body.

Transport in humans

In mass flow, fluid moves in response to a pressure gradient, flowing from a region of high pressure to regions of low pressure. Any suspended and dissolved substances present in the fluid move along the same direction.

Blood

Blood component	Main features
Plasma	- Main component of the blood - Consists largely of water. - Contains fibrinogen (blood-clotting) - Contains a wide range of substances to be transported.
Erythrocytes (red blood cells)	- Look like biconcave discs - Contain haemoglobin, a red pigment which carries oxygen and gives them their colour. - Mature erythrocytes do not contain a nucleus
Leucocytes (white blood cells)	- Larger than erythrocytes - Contain a nucleus and colorless cytoplasm - Have several types - Their main function is to defend the body against infection.
Platelets	- Tiny fragments of large cells called megakaryocytes. - Involved in the clotting of the blood.

The main functions of blood

- transports digested food products
- transports excretory products
- transports chemical messages (hormones)
- helps to maintain a steady body temperature
- acts as a buffer to pH changes.
- covers wounds with blood clots
- defends against disease.

Circulation systems

Many animals have a circulatory system in which a heart pumps blood around the body. Insects have an open circulatory system whereas most larger animals have a closed circulatory system with the blood contained within tubes.

Animals such as fish have single circulation. Birds and mammals need far more oxygen than fish. They have to maintain a constant body temperature which is usually higher than their surroundings. For this reason birds and mammals possess the most complex type of transport system, known as a double circulation because it involves two circulatory systems:

- The systemic circulation: carries oxygenated blood from the heart to the cells of the body where the oxygen is used, and carries the deoxygenated blood back to the heart.
- The pulmonary circulation: carries deoxygenated blood from the heart to the lungs to be oxygenated, and carries the oxygenated blood back to the heart.

Benefits of double circulation

- Oxygenated and deoxygenated blood cannot mix.
- Fully oxygenated blood can be delivered quickly to the body tissue at high pressure.

The blood vessels

- Arteries
- Capillaries
- Veins

Arteries

Arteries carry blood away from the heart towards the cells of the body. All arteries carry oxygenated blood except:

- pulmonary artery
- umbilical artery

The diameter of the lumen gets smaller in an artery further it is from the heart. The very smallest branches of the arterial system, furthest from the heart, are the **arterioles**.

aorta →

- Contain a lot of **elastic fibres** so they can stretch to accomodate the greater volume of blood
- Contain a lot of collagen fibres to withstand the pressure.
- Contain a few smooth muscle tissue

medium-sized artery →

- Contain less elastic fibres
- Contain more smooth muscle
- Contain a lot of collagen fibres

arteriole →

- Contain a few elastin fibres and collagen fibres
- Contain more smooth muscle than aorta.

Capillaries

Arterioles feed into networks of capillaries. These are minute vessels that spread throughout the tissues of the body.

Capillaries have a very simple structure well suited to their function. Their walls are very thin, containing no elastic fibres, smooth muscle or collagen.

This helps them fit between individual cells and also allows rapid diffusion of substances between the blood and the cells. Blood in capillaries, also, flows slowly allowing time for diffusion of substances.

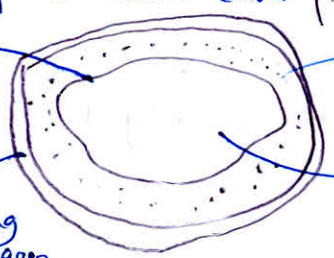
Veins

Veins carry blood back towards the heart. All veins carry deoxygenated blood except:

- the pulmonary vein
- the umbilical vein

Tiny venules lead from the capillary network, merging into larger and larger vessels leading back to the heart. Eventually, only two veins carry the blood back to the heart:

- the inferior vena cava from the lower parts of the body
- the superior vena cava from the upper parts of the body


smooth inner surface
relatively thin layer of smooth muscle with few elastic fibres
outer tough layer consisting mainly of collagen fibres
relatively large lumen

There are two main ways in which blood at low-pressure is returned back to the heart:

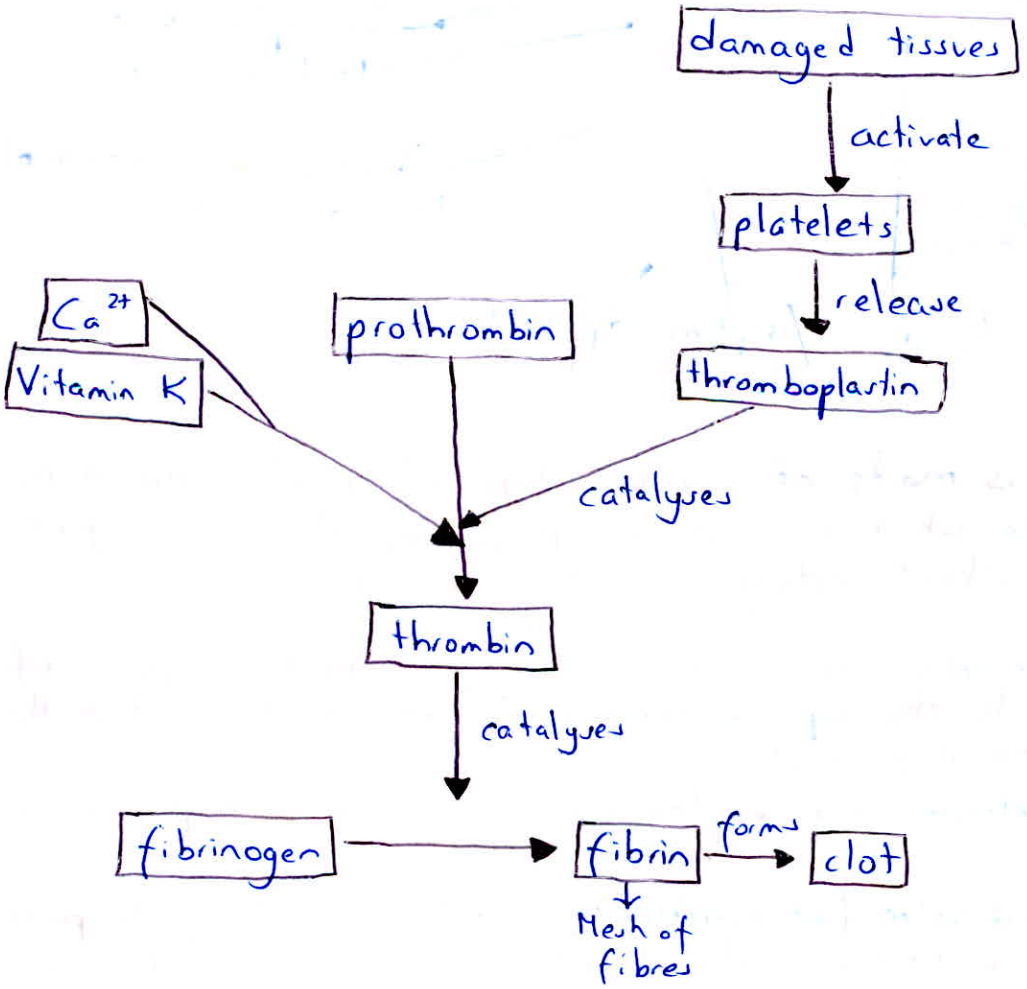
- Veins contain semilunar valves at frequent intervals. Blood can pass through towards the heart, but if it starts to flow backwards the valves close, preventing this.
- Many of the larger veins are situated between the large muscle blocks of the body. When the muscles contract during physical activity they squeeze these veins. With the valves keeping blood travelling in one direction, this squeezing helps them to return the blood to the heart.

The blood-clotting mechanism

Blood-clotting plays an important role because:

- It prevents blood loss.
- It prevents pathogens from getting into your body through an open wound.

The mechanism

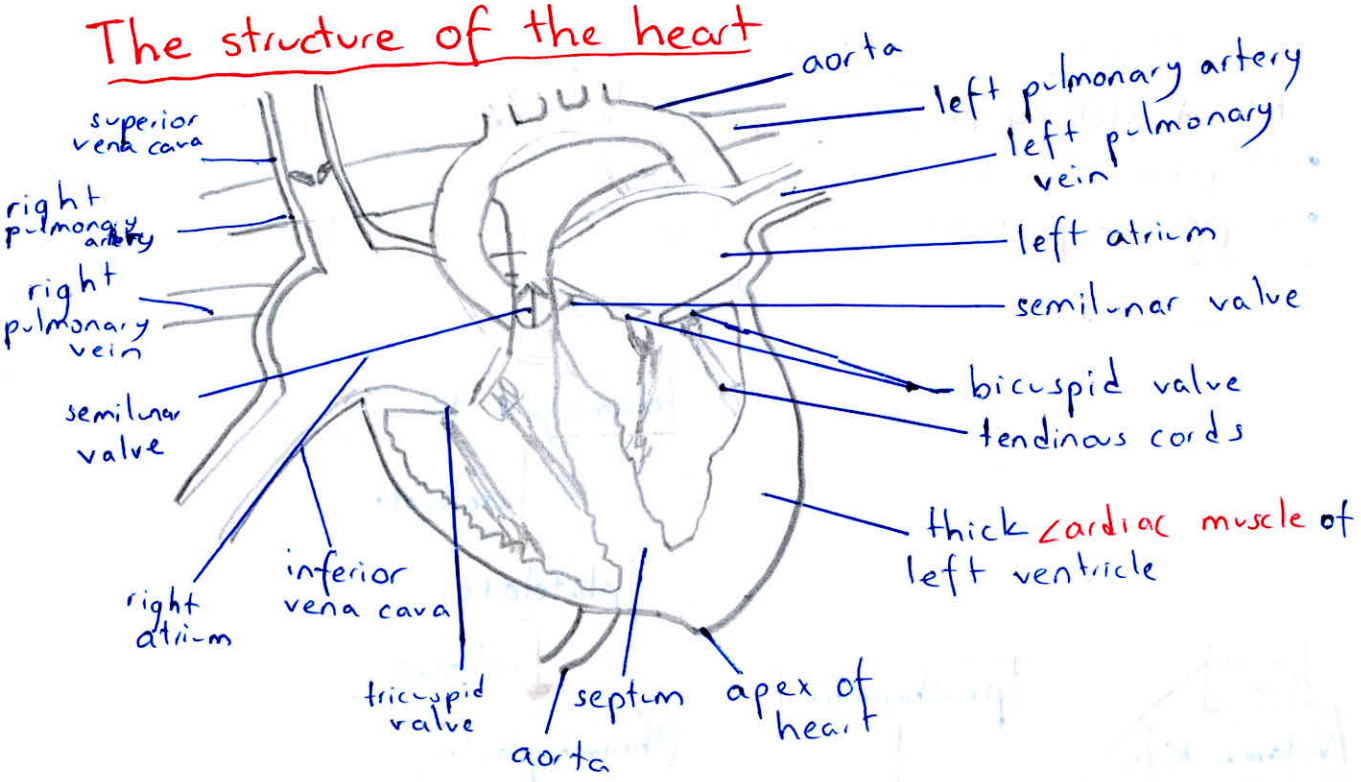


→ Thromboplastin catalyses the conversion of a large protein called prothrombin into another enzyme called thrombin. Calcium ions and vitamin K need to be present for this reaction to happen.

→ Thrombin acts on fibrinogen, converting it to a substance called fibrin. This forms a mesh of fibres.

→ More platelets and blood cells pouring from the wound get trapped in the fibrin mesh. This forms a clot.

The structure of the heart



* **The heart is made of** a unique type of muscle known as cardiac muscle which has special properties. It can carry on contracting without resting or getting fatigued.

- The inferior vena cava collects blood from the lower parts of the body, while the superior vena cava receives blood from the head, neck, arms and chest.
- The right atrium receives the blood and the blood passes to the ventricle.
- The tricuspid valve (atrioventricular valve) allows blood to pass from the atrium to the ventricle, but not in the other direction. The tough tendinous cords make sure the valves are not turned inside out by the great pressure exerted when the ventricles contract.
- The right ventricle is filled with blood under some pressure when the right atrium contracts. Then, the ventricle contracts forcing blood into the pulmonary arteries. Semilunar valves prevent the the backflow of blood.
- The blood returns from the lungs in the pulmonary veins. The blood returns to the left atrium. It contracts to force blood into the left ventricle. Backflow is prevented by the bicuspid valve.
- Left ventricle contracts to force blood out of the heart and into the aorta. Semilunar valves prevent the blood flowing back from the aorta into the ventricle.

The cardiac cycle

The heart continuously contracts and then relaxes. The contraction of the heart is called a systole. Systole can be divided into:

- atrial systole, when the atria contract together forcing blood into the ventricles, and
- ventricular systole, when the ventricles contract forcing blood out of the ventricles into the pulmonary artery and the aorta.

*Between contractions the heart relaxes and the atria fill with blood. This relaxation is called diastole. One cycle of systole and diastole makes up a single heartbeat. This is known as the cardiac cycle.

Atherosclerosis

Atherosclerosis is a cardiovascular disease (CVD) and it literally means hardening of the arteries, and is a build-up of plaques (yellowish fatty deposits).

Course of events

- Endothelial damage: Damage to the endothelial lining of blood vessels can be caused by several factors, such as high blood pressure and chemicals in tobacco smoke. Atherosclerosis usually occurs in arteries as the blood in arteries flows fast under relatively high pressure, which puts more strain on the endothelial lining.
- Inflammatory response: Once the damage has occcred, the body's inflammatory response begins and leukocytes arrive at the site of the damage. These cells accumulate chemicals from the blood, in particular cholesterol which leads to a fatty deposit known as atheroma forming on the endothelial lining of the artery.
- Plaque formation: Fibrous tissue and calcium salts also build up around the atheroma, turning it into a hardened plaque.
- Raised blood pressure: The lumen of the artery becomes much smaller as a result of the plaque. This increases the blood pressure, making it harder for the heart to pump blood around the body. The artery may bulge and the wall of the artery may become severely weakened, because it is under more pressure than usual. This is known as an aneurysm.

Keep up the good work.

19.10.15

Epidemiology

Example 1

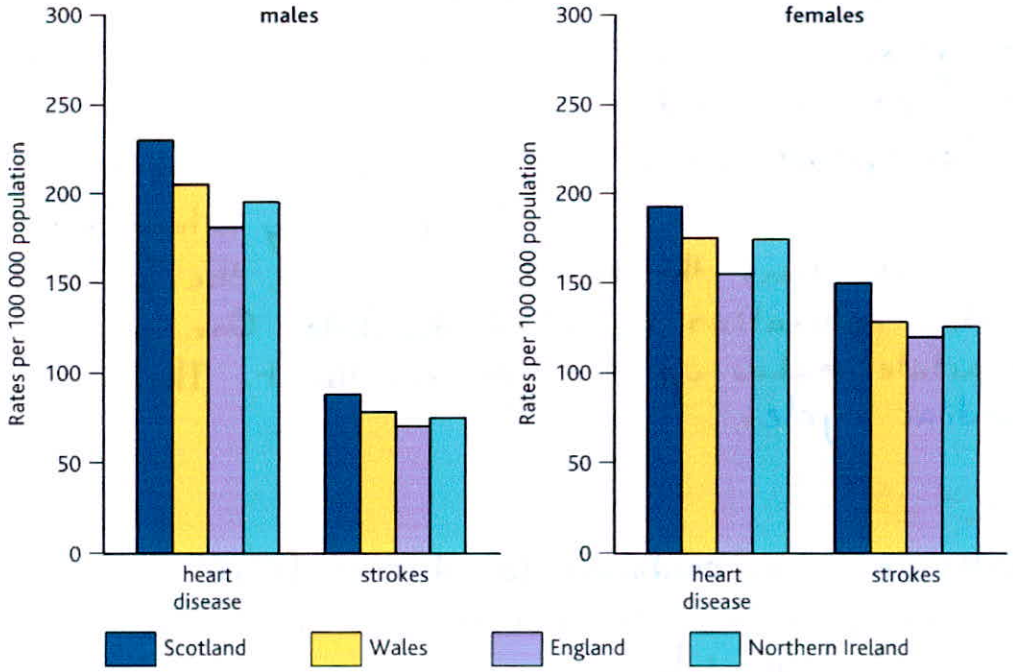
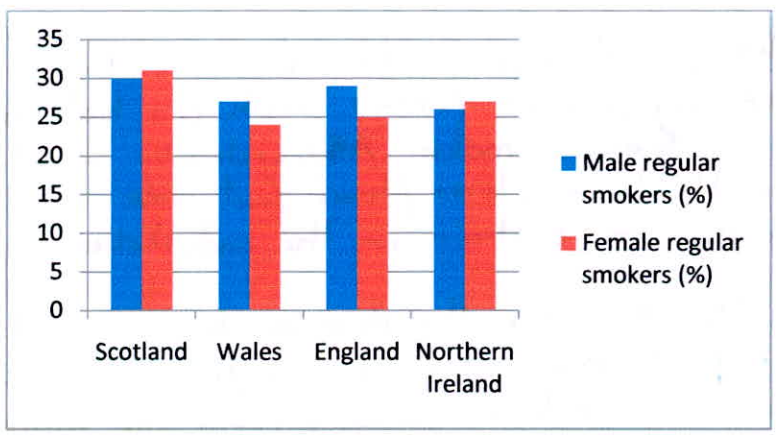


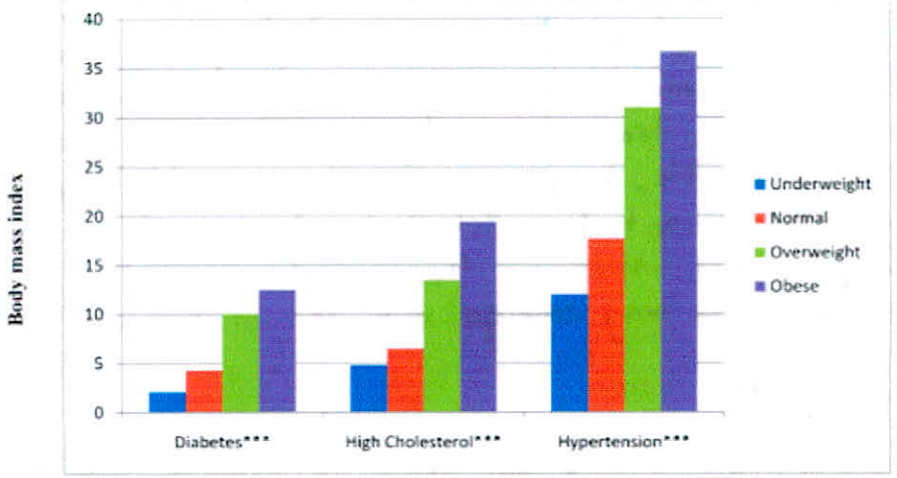
fig. 1.4.2 The numbers of deaths caused by two types of CVD.



→ The first bar graph illustrates the number of deaths caused by heart diseases and strokes while the latter displays the percentage of men and women who smoke regularly in different areas of the UK.

→ There seems to be a similarity between the mortality from heart disease or stroke and smoking patterns, suggesting a correlation between the two, that is a link. For instance, smoking is most popular in Scotland for both genders and deaths caused by CVD is most common. 30% of the male population smoke in Scotland while 29% of the male population smoke in England. Although you would expect the number of deaths caused by CVD in England to be close to the number of people dying in Scotland, the deaths caused by CVD is much less in England which is a conflicting evidence. Another conflicting evidence is the fact that ~~the~~ relatively the least proportion of the population smoke in Northern Ireland, yet mortality rate is higher than of England. This suggests that other factors such as genetic factors and air pollution may be causing the mortality rates. Therefore, further research needs to be done to establish a causal link between smoking and CVD. Correlelation is not the same as causation.

Example 2



→ The bar chart illustrates the number of people affected by three different diseases who are of different body masses.

→ There seems to be a positive correlation between increasing body mass and risk of disease. Underweight people have the lowest risk of getting one of this diseases whereas obese people have the highest risk. There is no conflicting evidence, so we might say there is a causal link between body mass and the risk of these three diseases.

Perceived risk and actual risk

Risk describes the probability that a particular event will happen. The actual risk of doing something is not always the same as perceived risk. Perception of risk is based on a variety of factors which include familiarity with an activity, how much you enjoy the activity and whether you approve of it. The mathematical risk may play very little part in building up your personal perception of risk.

There are other reasons that result in the misjudging of risk. Some people will continue smoking because they don't want to put on weight. Here the health risks of obesity are overestimated in comparison with those of smoking, or the risks of smoking are ignored.

Peer pressure, personal experience and fatalism all affect the desire of people to change their behaviour.

Epidemiological studies and CVDs

Most epidemiological studies are longitudinal studies and are based on a very big sample size. Longitudinal studies are very valuable because they follow the same group of individuals over many years. This means the impact of their known lifestyle on their health can be tracked over time. The ideal is to investigate one factor or variable, keeping all other variables controlled, however variables cannot be controlled when working with human beings. Despite this increasing the sample size, the more likely it is that patterns may emerge and the study will be more accurate.

Evaluation of the studies

When considering a study you need to examine the methodology to see if it is valid, that is, properly designed to answer the questions being asked. You also need to see if the measurements have been carried out with precision. It is important to find out if other scientists have been able to repeat the methodology and have had similar results. If so, the results are considered more reliable. It is also important to know who carried out the research, who funded it and where was it published, and decide whether any of these might have biased the study.

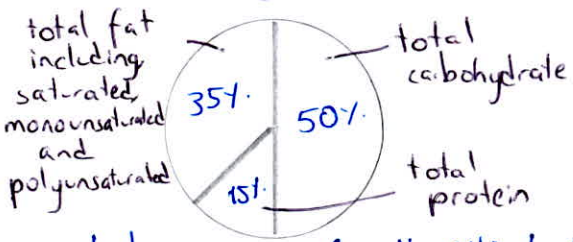
A balanced diet

The right balance of food in your diet is central to your health. If you eat too little food (undernutrition) or too much (overnutrition) over a period of time then you may suffer from malnutrition.

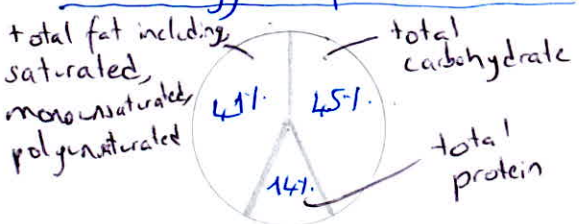
- Undernutrition can reduce resistance to disease and shorten lifespan. People, who are seriously underweight cannot get sufficient essential amino acids, minerals and vitamins and so suffer deficiency diseases.

- Overnutrition can also create many health problems. If more energy is taken in than is required, the excess is stored as fat and obesity may result. Obesity is a rapidly increasing problem, mainly in the developed world, such as in the UK.

suggested energy mix for the UK diet



actual energy mix for the UK diet



→ Carbohydrates, proteins and lipids, along with any alcohol in the diet, provide us with energy. There is some evidence that the proportion of energy-giving foods in the diet can increase or decrease the likelihood of problems such as heart disease developing. When compared with suggested dietary reference values (DRVs), UK population is eating food that contains too much energy, not enough vitamins and minerals and too much fat.

The energy budget

* The amount of energy contained in a food can be measured using a process known as calorimetry.

Energy budget

basal metabolic rate (BMR) | physical activity level (PAL)

- Basal metabolic rate: The energy needed for the basic metabolic reactions of the body to take place. The BMR is related to the total body mass and the lean body mass. People with a high proportion of muscle will have a higher BMR because muscle tissue requires more energy for maintenance than fat. This is one reason why men usually have higher BMRs than women.
- Physical activity level: A factor which represents the level of activity undertaken by an individual.

* Multiplying BMR with PAL gives the estimated average requirement. (EAR).

* If your energy intake and energy requirements are the same, your energy balance will mean that you neither gain or lose weight.
* If you do not match your energy intake to the requirements of your body then you will either gain weight or lose weight.

Body mass index (BMI) gives an indication about your mass-to-height ratio and epidemiological studies have correlated it with the risk of developing CVDs.

Developing obesity

A report suggests that the change in energy balance is linked to modern lifestyles rather than to simply poor individual choices. Energy-rich food is widely available and cheap. Modern lifestyles include little exercise. So as the average energy input has increased the energy output has fallen and people are gaining weight. Obesity levels are therefore rising.

- Solutions:

- Include a tax on fatty foods
- Town planning to make walking and cycling easier
- Educating children to prevent childhood obesity

* Are these solutions ethical?

Risk factors for CVDs

CVDs are multifactorial. A multifactorial disease is a disease that is the result of many factors. For CVDs, these factors fall into two main groups- those you can't help and those you can do something about.

- Three main risk factors for CVDs which cannot be altered:

• Genes: Studies, especially identical twin studies, have shown there is a great tendency in some families and in some ethnic groups to develop CVDs.

• Age: As you get older, your blood vessels begin to lose their elasticity and to narrow slightly, making you more likely to suffer from CVDs, particularly heart disease.

• Gender: Statistically, under the age of 50, men are more likely to suffer from heart disease women. Oestrogen in females appears to reduce the build-up of plaque. This gives women some protection against CVDs until they go through the menopause and oestrogen levels fall.

- Lifestyle factors in CVDs which can be altered:

• Smoking

Studies have shown that smokers are far more likely to develop CVDs than non-smokers with a similar lifestyle.

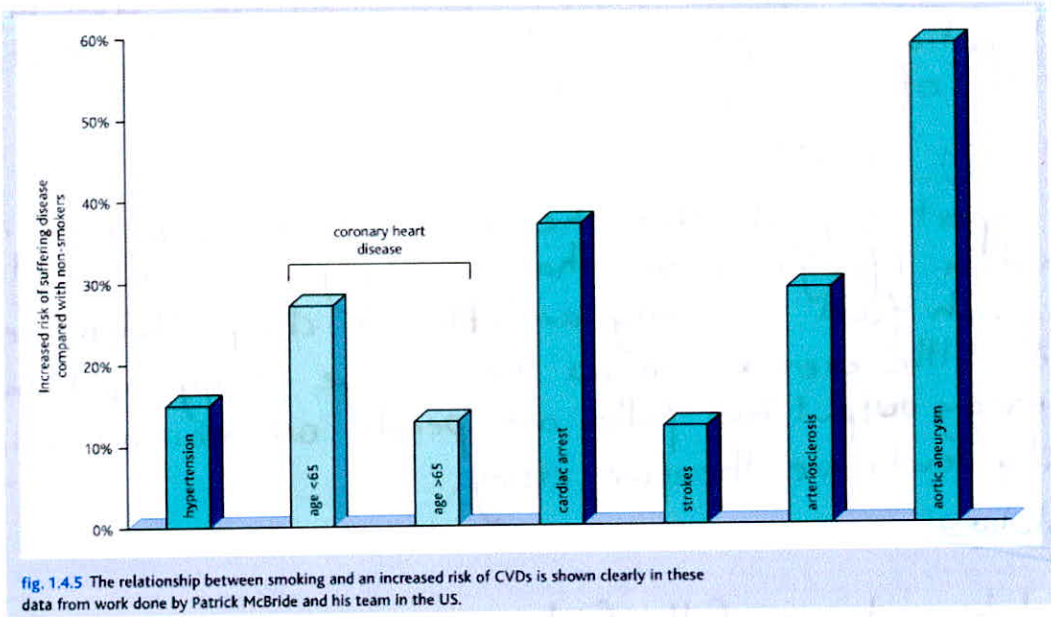


fig. 1.4.5 The relationship between smoking and an increased risk of CVDs is shown clearly in these data from work done by Patrick McBride and his team in the US.

The studies show a correlation between smoking and CVDs. Causation was established by further research. For example, studies found that some of the chemicals found in tobacco smoke can damage the lining of the arteries making the build-up of plaque more likely. Smoking also causes the arteries to narrow, raising the blood pressure and increasing the risk of CVDs.

- **Exercise**

Regular exercise can slow the heart rate, lower blood pressure, lower blood cholesterol levels and balance the lipoproteins in your blood. All of these lower your risk of CVDs.

- **Stress**

High stress levels increase the risk of cardiovascular disease by causing prolonged high blood pressure and a faster heart rate.

- **Weight**

Being overweight puts a greater strain on the heart because your heart has to work harder to move the blood through all the extra tissue. Recent studies have shown that the waist-to-hip ratio may be much better predictors of risk. The ratio of HDLs and LDLs should also be considered.

- **Diet**

There have been many studies on how diet is linked to CVDs, most of them looking at general diet. A study held in several countries showed that where people eat a lot of fatty meat and dairy foods (mostly saturated fats), many people die of heart disease. This suggests that high levels of saturated fats in the diet may be a risk factor.

The link between a diet high in saturated fats and a raised incidence of CVDs shows a correlation, but not a cause.

* A high intake of saturated fats is associated with high blood cholesterol levels. Cholesterol is involved in plaque formation in atherosclerosis, so this suggested a cause for the link between a high-fat diet and CVDs.
* Further studies have associated two types of lipoproteins with CVDs.

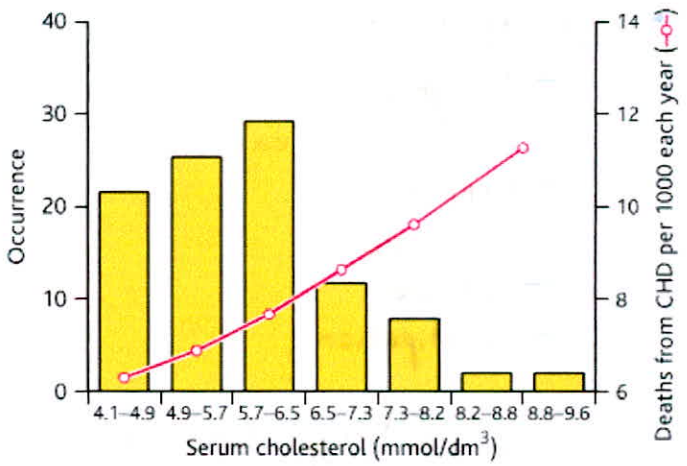


fig. 1.4.9 The relationship between blood cholesterol levels and death from coronary heart disease in men in the UK. The bars show the frequency with which the different cholesterol concentrations are found, while the line graph shows the number of heart attacks per 1000 men each year.

- **Low-density lipoproteins (LDLs)** are formed from saturated fats, cholesterol and protein. They carry more cholesterol than HDLs. If your LDL levels are high, your cell membranes become saturated and so more LDL cholesterol is left in blood.
- **High-density lipoproteins (HDLs)** are formed from unsaturated fats, cholesterol and protein. They carry cholesterol from your body tissues to your liver where it is broken down, lowering blood cholesterol levels. HDLs can even help to remove cholesterol from fatty plaques on the arteries, reducing the risk of heart disease from atherosclerosis.

The Benefits and Risks of treatments for CVD

People suffering CVDs are prescribed drugs which aim to reduce the risks associated with CVDs by helping to prevent problems developing. However, all medicines carry some risk.

- Controlling blood pressure

Drugs that reduce blood pressure are known as antihypertensives. There are several antihypertensives:

- Diuretics - increase the volume of urine produced. This gets rid of excess fluids and salts, so that the blood volume falls. With less blood, the blood pressure falls.
- Beta blockers - block the response of the heart to hormones, which normally act to speed up the heart and increase the blood pressure. So beta blockers make the heart rate slower and the contractions less strong, so the blood pressure is lower.
- Sympathetic nerve inhibitors - prevent the nerves stimulating the constriction of arteries, which helps to keep the arteries dilated and your blood pressure lower.

+ Risks of these drugs

The risks of these treatments are themselves twofold:

- Blood pressure of a person can become too low and that can lead to falls and injuries.
- Side effects of drugs:
  - Coughs
  - Swelling of ankles
  - Impotence
  - Tiredness
  - Fatigue
  - Constipation

However, antihypertensives are used as their benefits outweigh their risks.

24.10.15
Keep up the good work!

Statins

Statins are a group of drugs that lower the level of cholesterol in your blood. They block the enzyme in the liver that is responsible for making cholesterol and are particularly effective at blocking the production of LDLs. Statins also improve the balance of LDLs to HDLs and reduce inflammation in the epithelium of the arteries. Both of these functions reduce the risk of atherosclerosis developing. Most people use statins with little or no ill effect. Plant stanols and sterols are added to food which help to lower the cholesterol levels in the blood too.

Anticoagulants and platelet inhibitory drugs

Drug treatments are used to help prevent the blood clotting too easily. Here are two examples.

- Anticoagulants: Warfarin is an anticoagulant that interferes with the manufacture of prothrombin in the body. Low prothrombin levels make the blood clot less easily. In humans the dose is carefully monitored to make sure that the clotting of the blood is reduced but not prevented completely.
- Inhibitory drugs: Platelet inhibitor drugs make the platelets less sticky, and so reduce the clotting ability of the blood. The cheapest and most common of these is aspirin.

Prevention is better than cure

A lot of scientific evidence is used by the Government and health organisations to produce advice on how to improve our health.

Cardiovascular disease has a devastating impact on individuals, on families and on society. It costs a lot of money to treat people in hospital. While those people are too ill to work, they are not only losing money for their families, they are losing money for the companies they work for.

So, prevention is better than cure for CVDs for many reasons, but persuading people to change their lifestyle habits is difficult.

* Health education programmes can help to make sure that everyone is aware of the risks associated with different lifestyle choices, but each individual has to make their own choices and take their own risks.

Topic 2: Genes and health

Nucleic acids

Nucleic acids are the information molecules of the cell. The infamation is stored in the chromosomes in the nucleus of the cell. It takes the fom of a code in the molecules of DNA - deoxyribonucleic acid. Parts of the code are copied into one form of RNA- ribonucleic acid, then to another form, and finally used to make proteins that build the cell and control its actions.

Nucleotides

Nucleotides are the building blocks of nucleic acids. The single units are called mononucleotides. Each mononucleotide has three parts:

→ pentose sugar (deoxyribose or ribose)
→ phosphate
→ nitrogenous base (thymine, uracil, cytosine, adenine or guanine)

* The pentose sugar in RNA is ribose.
* The pentose sugar in DNA is deoxyribose.

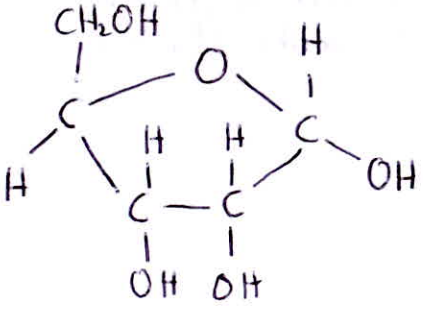
There are two types of nitrogen-containing bases found in nucleic acids.

→ The purine bases have two nitrogen-containing rings.
→ The pyrimidines have only one nitrogen-containg ring.

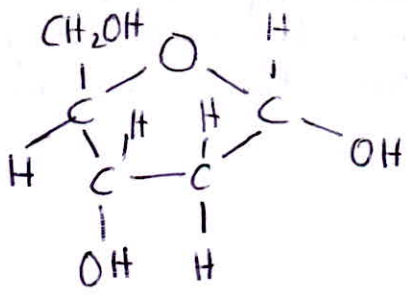
In DNA		In RNA	
purines	pyrimidines	purines	pyrimidines
• adenine —	• thymine	• adenine —	• uracil
• guanine —	• cytosine	• guanine —	• cytosine

* The sugar, the base and the phosphate group are joined together by condensation reactions with the elimination of two water molecules to form the nucleotide.

Ribose



Deoxyribose



Building the polynucleotides

Mononucleotides are themselves linked together by condensation reactions to form polynucleotide strands. The sugar of one nucleotide bonds to the phosphate group of the next nucleotide so a phosphodiester bond forms and the phosphate is combined with carbon-3 of one ~~group~~ deoxyribose and carbon-5 of the next.

RNA molecules form single polynucleotide strands which may be folded into complex shapes or remain as long thread-like molecules. A DNA molecule is made up of two polynucleotide strands, twisted around each other.

* In DNA, a purine always pairs with a pyrimidine. This results in the famous DNA double helix.

The two strands of the double helix are held together by hydrogen bonds between the complementary base pairs. The two strands are antiparallel.

guanine ≡≡≡ cytosine (3 hydrogen bonds)

thymine ≡≡≡ adenine (2 hydrogen bonds)

DNA replication

Replication plays an important role in passing on information to the next generation.

-Process

- The chains of nucleotides fit together perfectly in double helix, as long as cytosine and guanine, adenine and thymine are always matched together.
- When the DNA replicates, the two strands of the DNA molecule unzip along the line of hydrogen bonds and unravel. This is brought about by the enzyme DNA helicase. The strands act as templates for the new DNA strands.
- The exposed bases attract free DNA nucleotides and new hydrogen bonds are formed between matching base pairs. The enzymes DNA polymerase and DNA ligase join the nucleotides together to form new DNA strands.
- The result is two strands of DNA identical with the original piece. The new molecules automatically coil up into the double helix as weak hydrogen bonds form within the structure.

* This process is semi-conservative. Semi-conservative replication: The process by which two copies of a DNA molecule are made and in which both parent strands remain intact and act as templates for the formation of new complementary strands. Meselson and Stahl's experiment supports this theory.

The experiments of Meselson and Stahl

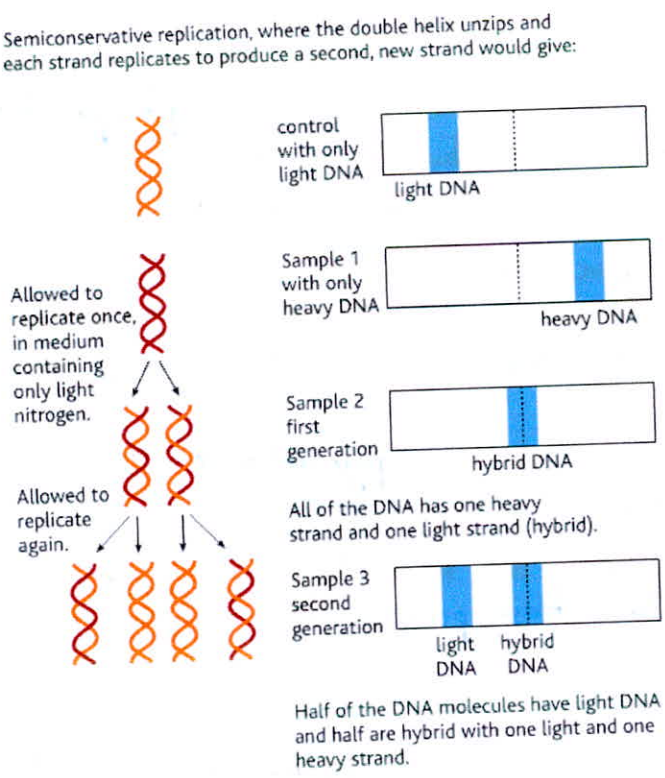

Semiconservative replication, where the double helix unzips and each strand replicates to produce a second, new strand would give:
control with only light DNA
light DNA
Sample 1 with only heavy DNA
heavy DNA
Allowed to replicate once, in medium containing only light nitrogen.
Sample 2 first generation
hybrid DNA
All of the DNA has one heavy strand and one light strand (hybrid).
Allowed to replicate again.
Sample 3 second generation
light DNA
hybrid DNA
Half of the DNA molecules have light DNA and half are hybrid with one light and one heavy strand.

fig. 2.1.8 After Meselson and Stahl produced their evidence, support for the idea of conservative replication melted away.

→ Meselson and Stahl have confirmed the Watson and Crick hypothesis on DNA replication by a classic series of experiments.

The experiment

- They grew several generations of E.coli in a medium wheir their only source of nitrogen was the radioactive isotope ^{15}N. Atoms of ^{15}N are denser than those of ^{14}N. The bacteria grown on this medium took up the radioactive isotope. After several generations all the bacterial DNA was labelled with ^{15}N.
- The bacteria were then moved to a medium containing ^{14}N as their only nitrogen source, and the density of their DNA was tested as they reproduced.
- Meselson and Stahl predicted that if DNA reproduces by semi-conservative replication, then all of the DNA would have the same density halfway between that of ^{15}N- and ^{14}N- containing DNA.

The nature of the genetic code

In a double helix of DNA, the components that vary along the structure are the bases. So scientists guessed that it was the arrangement of the bases that carries the genetic code. However, if one base coded for one amino acid, there could be only four amino acids which is not the case. They came up with a triplet code. A triplet code of three bases of DNA code for a single amino acid.

Each sequence of three bases along a strand of DNA codes for something very specific. Most code for a particular amino acid, but some triplets instead signal the beginning or the end of one particular amino acid sequence.

TAC → Met/start

ATT and ATC → End

* A sequence of three base pairs on the DNA or RNA is known as a codon.

- A gene: A gene is usually defined as a sequence of bases on a DNA molecule coding for a sequence of amino acids in a polypeptide chain.

Protein synthesis

RNA is closely related to DNA but it does not form enormous and complex molecules like DNA. Different types of RNA play different roles in the process of protein synthesis.

- Messenger RNA (mRNA): caries information from the DNA in the nucleus out into the cytoplasm. It is formed when a small length of the DNA double helix unzips. The coding or antisense strand of the DNA acts as a template for the formation of the mRNA. The mRNA then moves out of the nucleus, transporting the instructions from genes to the surface of the ribosomes which are the sites of protein synthesis.

- Transfer RNA (tRNA): is found in the cytoplasm. It picks up a particular ~~protein~~ amino acids. The tRNA molecules, each carrying an amino acid, line up alongside the mRNA on the surface of the ribosome, building up a long chain of amino acids. Peptide links are formed between the amino acids, joining them together to form a polypeptide chain which in turn can be used to form a larger protein.

Process:

1- The DNA is transcribed to give a length of mRNA. Transcription: The process by which the DNA nucleotide base sequence of a gene is copied into the RNA nucleotide base sequence in a molecule of messenger RNA.

2- a) mRNA moves out of the nucleus through nuclear pores and becomes engulfed by a ribosome.

b) tRNA in the cytoplasm attaches to specific amino acids.

3- tRNA molecule carrying amino acid lines up against matching mRNA on the ribosome. It is translated.

4- Peptide links are formed between the acids brought by the tRNA.

5- When the polypeptide is released into the ~~cytop~~ cytoplasm, the tRNA units also unbind and return to the cytoplasm to pick up more amino acids. The ribosome may read the mRNA again.

- Translation: Process by which the genetic code is converted into new protein molecules directed by RNA.

Mutation

The genetic code carried on the DNA is translated into living cellular material during protein synthesis. The nucleic acids are central to the process, as both the carriers and the translators of the genetic code. If a single codon is changed or misread during the process, then the amino acid for which it codes may be different, and so the whole polypeptide chain and indeed the final protein may be altered. Hence, mutation is defined as rare, random change in DNA.

Many of the genetic diseases are the result of these random mutations in the genetic material of the gametes. Examples include cystic fibrosis, in which a membrane protein does not function properly.

There are different types of mutations:

- Chromosomal mutations involve changes in the position of genes within the chromosomes.

- Point mutation - Gene deletion - Duplication - Inversion - Translocation

- Whole-chromosome mutations: where an entire chromosome is either lost during meiosis or duplicated in one cell by errors in the process. For example, Down's syndrome is caused by a whole-chromosome mutation.

The basics of inheritance

- Gene: A meaningful segment of DNA coding for a particular protein or polypeptide.
- Allele: Different versions of a gene that produce variations of the characteristic.
- Genotype: The genetic information of an individual organism
- Phenotype: The set of observable characteristics of an individual resulting from the interaction of its genotype with its environment
- Recessive: Alleles that are only expressed in the phenotype when no dominant allele is present.
- Dominant: Alleles that are expressed in the phenotype even a recessive allele is present.

* If both alleles coding for a particular characteristic are identical, then the organism is homozygous for that characteristic - it is a homozygote.
* If the two alleles coding for a characteristic are different, the organism is heterozygous for that characteristic and is called a heterozygote

- Monohybrid cross: When one gene is considered at a time in a genetic cross, it is referred to as a monohybrid cross.

Carrying out genetic experiments

A suitable organism for a genetic experiment should, ideally, have the following features:

- be relatively easy and cheap to raise, to maximise the chance of successful breeding and minimise the cost of the experiment
- have a short life cycle so that the results of crosses and/or mutations can be seen quickly
- produce large numbers of offspring
- have clear, distinguished characteristics

-Sampling errors:

- some offspring dying before they can be sampled
- inefficient sampling techniques
- chance plays a great role in reproduction - the joining of particular gametes is a completely random affair, unlike the theoretical diagrams drawn.

* The smaller the sample, the larger the potential sampling error.

Understanding human genetic traits

Thalassaemia

Thalassaemia is not a single disorder - there are range of thalassaemias and they all affect the polypeptide chains of the haemoglobin molecule, which carries oxygen in the blood.

Haemoglobin shows polygenic inheritance, with a different gene coding for each of the two different chains. Depending on the type of disease, thalassaemia prevents the formation of either the alpha or beta haemoglobin chains. It has several symptoms but they all include anaemia.

Thalassaemia cannot be cured. It can be treated by regular blood transfusions, but the body builds up an excess of iron, so drugs are needed to deal with this problem too.

Luckily, it is inherited by a recessive allele

* Some countries where thalassaemias are very common have introduced screening programmes to try and reduce the numbers of affected children born.

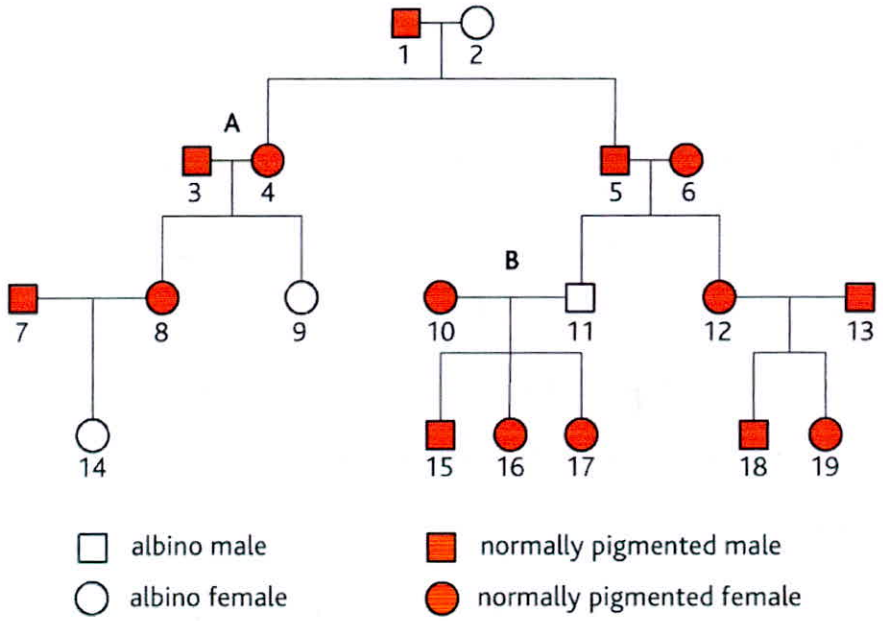
Genetic pedigree diagrams

A family tree or genetic pedigree diagram includes all the members of a family, indicating their sex and whether or not they have the disease.

In families affected by conditions such as thalassaemia and cystic fibrosis, genetic pedigree diagrams can be useful in protecting which family members may be carriers of the genetic mutation, allowing them to consider their options before they conceive a child.

The Albino trait

Albinism is a condition in many species in which the natural melanin pigment of the skin, eyes and hair does not form. Albinism is inherited through a recessive allele. The parents may appear normal - in which case they are both carriers of the albino allele - or one or more of the parents may be an albino themselves.



Diffusion and gaseous exchange

Decreasing surface area to volume makes it increasingly difficult for diffusion to supply materials fast enough to cells as the size of the organism increases. This is why large organisms, such as animals, have a respiratory system.

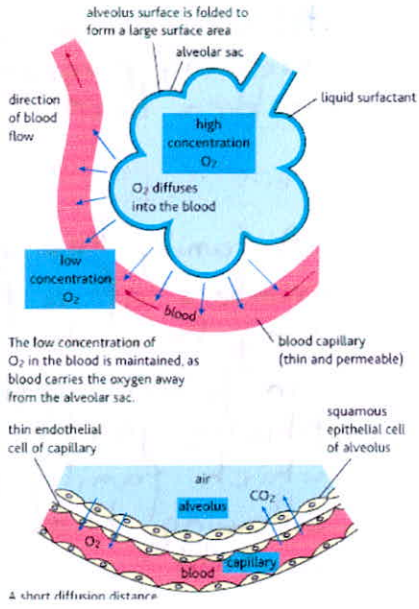
The human respiratory system

It includes the chest and mouth and nose. The nasal passages have a good blood supply, and the lining secretes mucus and is covered in hairs. This means that the external air is prepared before entering the rest of the system.

- Gas exchange in alveoli

An alveolus is made of a single layer of flattened epithelial cells. The capillaries that run close to the alveoli also have a wall which is only one cell thick. Between the two is a layer of elastic connective tissue holding everything together. The elastic tissue helps to force air out of the lungs, which are stretching when you breathe in. This is known as the elastic recoil of the lungs.

Gaseous exchange occurs by a process of simple diffusion between the alveolar air and the deoxygenated blood in the capillaries.



Adaptations of alveoli

- **Large surface area** – The bigger the surface area the more particles can be exchanged at the same time. The alveoli provide an enormous surface area for the exchange of gases in the human body.
- **Short diffusion distance** – The walls of the alveoli are only one cell thick, as are the walls of the capillaries that run beside them.
- **Steep concentration gradient** – Blood is continuously flowing through the capillaries past the alveoli, exchanging gases. The continuous flow of the blood maintains the concentration gradient on the capillary side. The air within the alveoli is constantly being refreshed with air from outside by breathing.

– **To memorise** – Fick's law:

$$\text{rate of diffusion} \propto \frac{\text{surface area} \times \text{concentration gradient}}{\text{thickness of exchange membrane}}$$

Breathing

• Inhalation

Inhalation is an active, energy-using process:

+ The muscles in the diaphragm contract.
+ As a result, it is lowered and flattened.
+ The intercostal muscles between the ribs also contract.
+ The rib cage is raised upwards and outwards
+ Volume of the chest cavity increases.
+ Hence, the pressure in the cavity decreases.
+ Air moves in.

• Exhalation

Normal exhalation is a passive process:

+ The muscles surrounding the diaphragm relax so that it moves up into its dome shape.
+ The intercostal muscles also relax.
+ So, the ribs move down and in, and the elastic fibres around the alveoli return to their normal length.
+ Volume of the chest cavity decreases.
+ The pressure in the cavity increases.
+ Air moves out.

pressure outside > pressure inside

* Air moves <u>in</u>.

pressure outside < pressure inside

* Air moves <u>out</u>.

Transport proteins in action

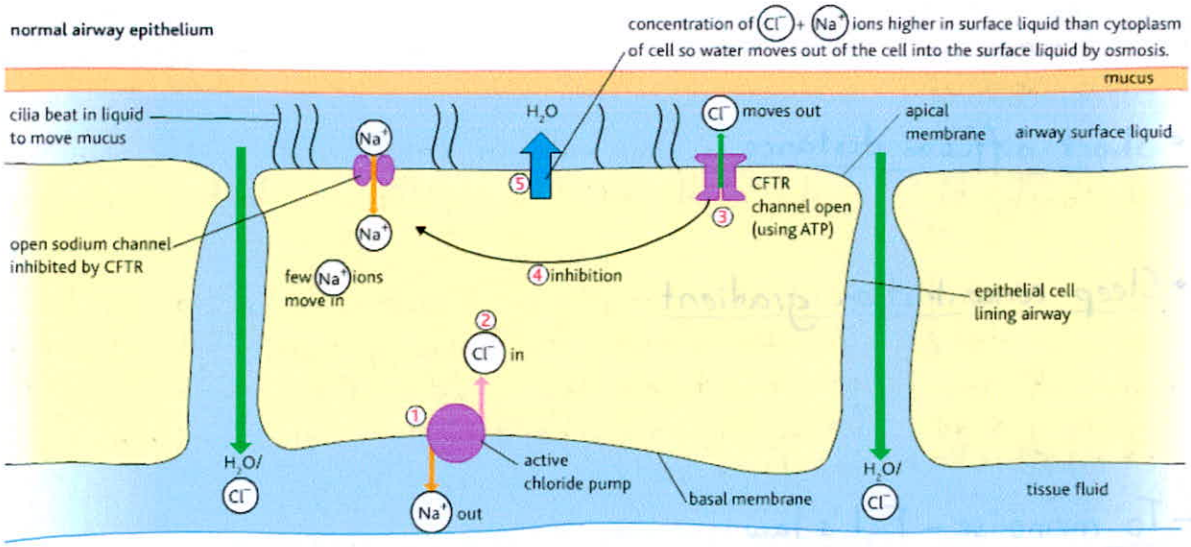


fig. 2.3.19 This complex process keeps the mucus produced by the epithelium lining your airways really runny. This helps your body prevent infection and also keeps the airways from getting blocked.

(1) Chloride ions are actively transported into the epithelial cells that line the respiratory tubes from the tissue fluid surrounding them. This transport system is known as a chloride pump.

(2) As a result of this pump, the chloride ion concentration in the epithelial cells lining the airways is high. This creates a concentration gradient between the cell contents and the fluid on the surface of the epithelium inside the airway.

(3) Chloride ions diffuse out of the cells into the fluid in the airways. They pass through chloride channels in the membrane that lines the lumen of the airway. The proteins that form these channels are known as the cystic fibrosis transmembrane regulatory channel proteins. (CFTR)

(4) When CFTR channel is working, it inhibits the movement of sodium ions ~~in the fluid lining~~ into the cell through the sodium channels. As a result, the concentrations of sodium and chloride ions in the fluid lining the airways are higher than the concentrations of the solutes in the cytoplasm of the epithelial cells. Water moves out of the cells into the fluid lining the airways by osmosis.

(5) The water that moves out of the epithelial cells by osmosis mixes with the mucus which is also produced by cells in the epithelial layer and keeps it runny so that it can be moved easily by the cilia.

* A similar process takes place in the epithelial cells that line your gut and your reproductive system whether you are female or male. Runny mucus is important in both. It keeps the narrow ducts and tubes open along which enzymes pass from the pancreas into your gut for example. It also makes the movement of sex cells in the reproductive system possible.

Cystic fibrosis

Cystic fibrosis is a serious, life-threatening condition that causes severe respiratory and digestive problems as well as very salty sweat and often infertility.

* The chloride transport systems of exocrine glands, including:
  - mucus secreting glands of + the lungs
    + the gut
    + the reproductive system
    + the sweat glands

don't function properly. As a result thick sticky mucus and very salty sweat are formed. It is the thick mucus which causes most of the symptoms.

* A faulty or absent CFTR causes cystic fibrosis. The gene that codes for it is so large. A mutation in any part of the gene can affect the CFTR protein and so cause cystic fibrosis.

Since, people with CF lack CFTR proteins

- Chloride ions build up in their cells instead of moving out through the channels
- As a result water does not move out of their cells to dilute the mucus on the surfaces of their membranes.
- Water moves into the cells by osmosis from the fluid surrounding the cells, making the mucus even more thicky and sticky.

Symptoms of cystic fibrosis

- The respiratory system

The thick, sticky mucus typical of cystic fibrosis builds up in the tiny airways of the lungs and reduces the flow of air into the alveoli. It often blocks the smaller bronchioles completely and greatly reduces the surface area available in the lungs for gaseous exchange.

They often have severe coughing, feel breathless and are often short of oxygen making them feel tired.

Bacteria and other pathogens that are breathed in and trapped in the mucus cannot be removed. They may cause serious infections.

- The digestive system

The enzymes from the pancreas are very important in the breakdown of carbohydrates, proteins and fats in the duedonum. The enzymes pass from the pancreas into your duedonum along a tube known as the pancreatic duct. Thin mucus is produced by the cells lining this tube in the same way as it is produced in the pancreatic duct is also very thick and sticky. It often blocks the pancreatic duct, so that the enzymes do not reach the duedonum.

This has two damaging effects:

- Digestive enzymes do not reach your gut
- Pancreas starts to digest itself.

No insulin = diabetes

* Not only does the thick mucus stop enzymes getting to the gut to digest food, it also makes it more difficult for any digested food to be absorbed into the blood.

- The reproductive system

The thick, sticky mucus produced in cystic fibrosis can have a damaging effect on the reproductive system.

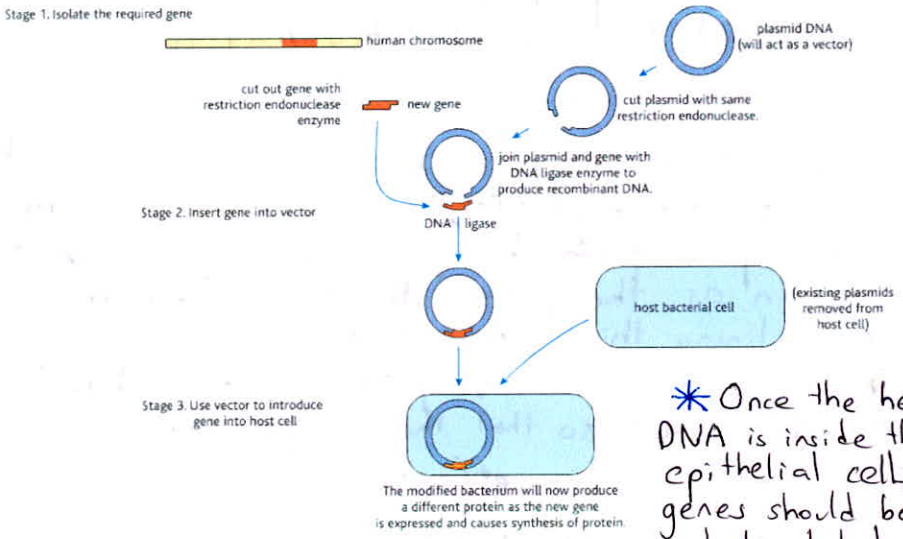
- Women with cystic fibrosis usually produce fertile eggs, but the thick mucus can block the cervix so sperm cannot reach them.
- Men with cystic fibrosis are often infertile. They may lack the tube that carries sperm out ~~of~~ from the testis into the semen. If the vas deferens is present, it may be partly or completely blocked by thick, sticky mucus so that only a reduced number of sperm can leave the testis.

Treating cystic fibrosis

- **Physiotherapy:** is very important for removing as much of the thick, sticky mucus from the lungs as possible.
- **Diet and enzymes:** Diet → high-energy foods, proteins
  Enzymes
- **Drug therapies:** Antibiotics, vaccines, mucolytics, asthma drugs, DNAase enzymes, insulin
- **Transplant surgery:** New organs will not be affected by CF. After a transplant, the person has to take immunosuppressant drugs for the rest of their life which suppresses the immune system.
- **Infertility treatments:** Women → IVF
  Men → Taking sperm and fertilisation in vitro

Gene therapy for cystic fibrosis

Gene therapy involves taking a copy of the healthy gene and finding an effective way of getting it into the cells that need it, so they can produce the correct protein.


Stage 1. Isolate the required gene
human chromosome
plasmid DNA (will act as a vector)
cut out gene with restriction endonuclease enzyme
new gene
cut plasmid with same restriction endonuclease.
join plasmid and gene with DNA ligase enzyme to produce recombinant DNA.
Stage 2. Insert gene into vector
DNA ligase
host bacterial cell
(existing plasmids removed from host cell)
Stage 3. Use vector to introduce gene into host cell
The modified bacterium will now produce a different protein as the new gene is expressed and causes synthesis of protein.

* Once the healthy new DNA is inside the lung epithelial cells, the healthy genes should be transcribed and translated, producing the normal, active CFTR protein and relieving the symptoms.

Difficulties of gene therapy for CF

- **Extracellular barriers**

There are many barriers to overcome before the new DNA in the vectors can reach the epithelial cells of the airways. This is partly because cystic fibrosis blocks the airways, making it difficult for sprays to penetrate the lungs and partly because the surface is coated with thick, sticky mucus.

- **Intracellular barriers**

Once the vector is inside the cell, the next challenge is to get the new DNA into the right place. Vectors that have been tested for the treatment of CF include harmless viruses and liposomes. Viruses give better results.

- **Keeping the gene expression going**

The final problem is that even when the new gene is taken into the nucleus and transcribed, it doesn't work for long. Research teams are working onto make this permanent.

The ethics of gene therapy

The gene therapy under development for cystic fibrosis is carried out on normal body cells (somatic cells) and is so known as somatic cell gene therapy. This kind of therapy does not alter the fact that if someone with CF has a child they will pass on faulty genes. A potential solution to this problem is to alter the germ cells – the reproductive cells of the body.

This may sound like a good idea, but many other people are concerned. No one is yet sure of the effect on an early embryo of such an invasive intervention.

Whilst attempting to remove the risk of genetic diseases seems a very positive aim, it could be difficult to know where to draw the line. Some people would be tempted to alter their genes to change skin colour, reduce adult weight and increase intelligence.

Genetic screening

The screening may be carried out during pregnancy with the option of terminating the pregnancy if the fetus is affected by a severe genetic disorder, or it may be carried out on newborn babies ~~disorder, or it may be carried out~~ to identify any problems and give the best treatment as early as possible.

For some diseases whole populations are tested. This is known as genetic screening. Although it is expensive, the cost of screening is outweighed by the health benefits and lower costs of early treatment.

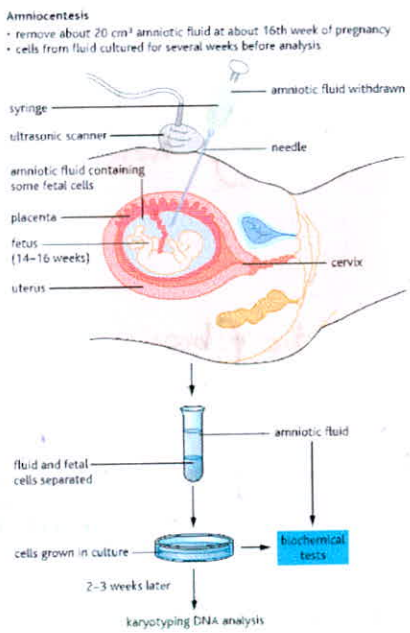
For families where the pedigree shows a history of an inherited disease, different screening tests can be offered to couples before they consider having a child. These tests offer help and hope but also lead to some very difficult choices.

Identifying carriers

It is possible to detect the CF allele in a carrier who has no symptoms. A sample of blood, or some cells from the inside of the mouth, can be used to carry out a simple test which identifies the allele.

Prenatal screening

Prenatal screening is testing a fetus for a genetic condition before birth. Parents, therefore, have the option of terminating pregnancy. To find out if a fetus has a genetic disorder, tests need to be carried out on some fetal cells. The fetal tissue can be obtained in one of two ways:



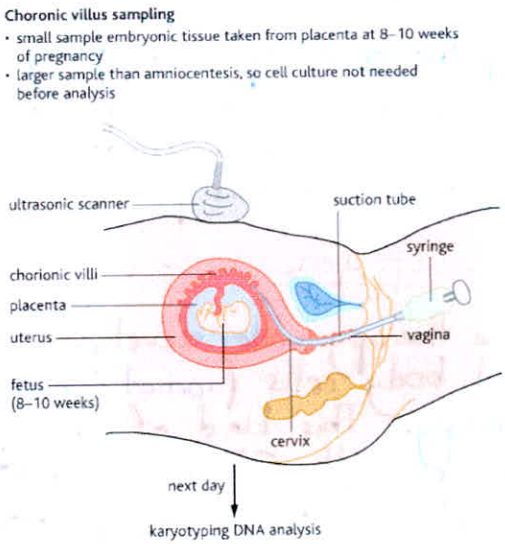


Fig. 2.4.14 Prenatal techniques like amniocentesis and chorionic villus sampling make an accurate diagnosis of cystic fibrosis and other genetic disorders possible before birth.

- **Amniocentesis**: Prenatal test that involves taking a sample of amniotic fluid at around 16 weeks of pregnancy and culturing the fetal cells to look for genetic abnormalities.

Disadvantages:

- It can only be carried out late in the pregnancy, so that should termination of the pregnancy be necessary it is more traumatic.
- The results are not available 2-3 weeks after the test.
- It carries a risk of spontaneous abortion.

- **Chorionic villus sampling**: Prenatal test for genetic disorders which involves sampling fetal tissue from the placenta at 10-12 weeks.

Disadvantages:

- There is a greater risk that the embryo may spontaneously abort after the tissue sample is taken, though the risk of miscarriage at this stage of pregnancy is much higher anyway.
- Any problems in the genes on paternal X chromosomes cannot be detected as they are inactivated in fetal placental cells.

Preimplantation genetic diagnosis (PIGD)

PIGD is a genetic diagnosis by which the genetic make-up of an embryo can be determined before it is implanted in the uterus of its mother. It is based on the technique of IVF (in vitro fertilisation). In this technique, the egg and sperm are fertilised outside the body. After a few cell divisions, a single cell is removed from each embryo. Amazingly, this causes no harm to the development of the embryo. The genetic make-up is checked and only those embryos free of the faulty alleles are placed in the mother's uterus to implant and grow.

* This method has the disadvantage that IVF is expensive and quite unreliable.

Making the right decision

Different people have different attitudes. Ethical frameworks can help us to make the 'best' decision.

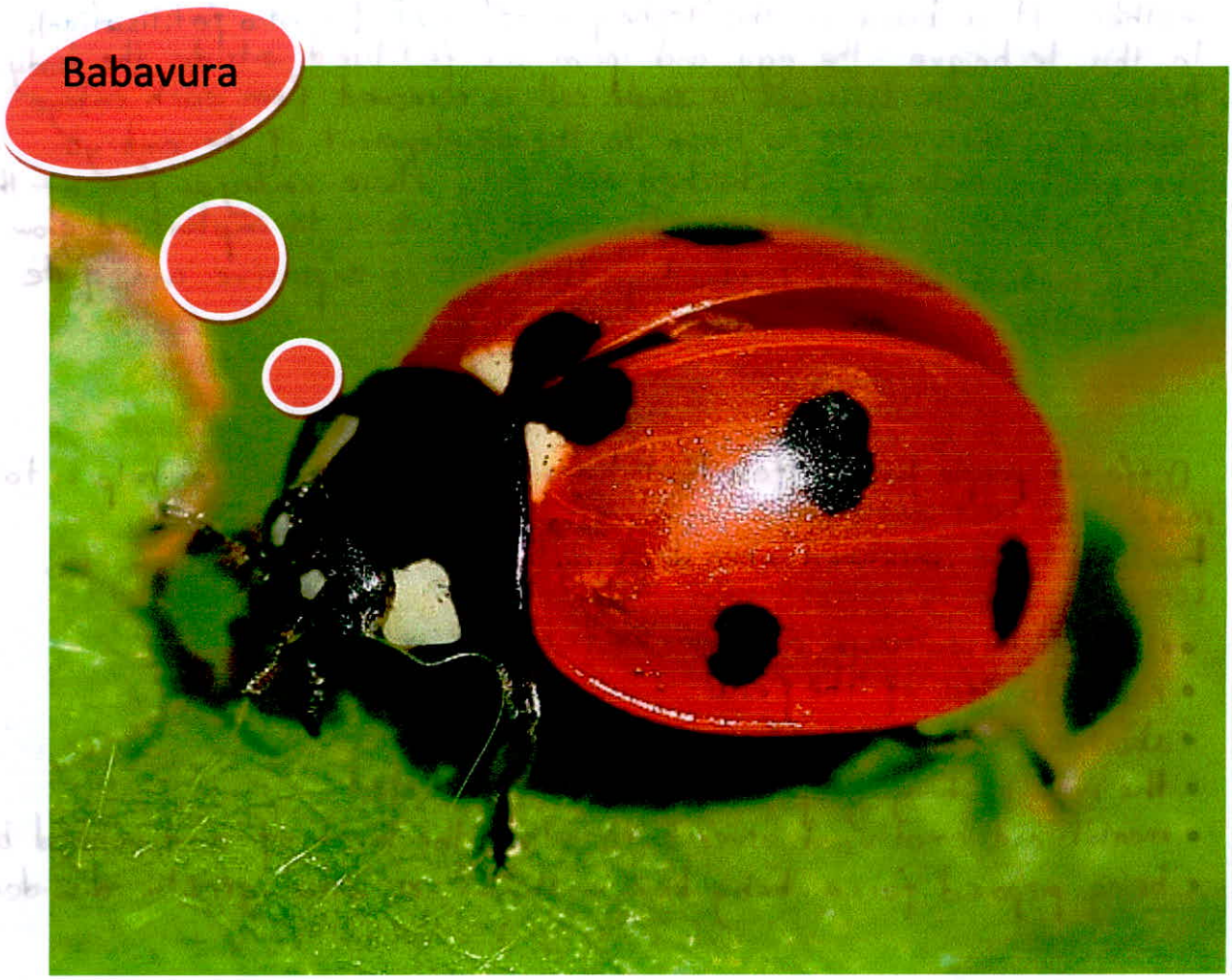
Factors to be considered when deciding what is 'best' in relation to screening are:

- risk of miscarriage or harm to fetus
- right to life of the fetus
- abortion in the event of a positive diagnosis
- the cost of bringing up a baby that is disabled
- mental and emotional issues surrounding the birth of a disabled baby.
- being prepared for a baby born with CF or other genetic disorder.

Keep up the good work!

Thank you...

07.12.15



- THE END -